

L11	1	10/151750 and (PEST or stability same (RNA or mRNA))	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:41
L12	0	10/151750 and (destabilizing)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:41
L13	0	10/151750 and (decrease adj5 stability)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:42
L14	1	10/151750 and (human)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:43
L15	292	li.in. and gfp	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:43
L16	5	li.in. and gfp same degrading	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:43
L17	0	li.in. and gfp same degrading and RNA adj5 stability	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:43
L18	0	li.in. and gfp same degrading and RNA adj5 stability	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:43
L19	3	li.in. and gfp same degrading and stability	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:44
L20	116	destabilizing adj5 (RNA or MRNA)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:44

L21	30	destabilizing adj5 (RNA or MRNA) and PEST	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:45
L22	2	destabilizing adj5 (RNA or MRNA) and PEST adj20 (Protein or peptide or polypeptide or sequence)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:47
L23	4	destabilizing adj20 (RNA or MRNA) and PEST adj20 (Protein or peptide or polypeptide or sequence)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:48
L25	317	AU adj rich or aubf	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:58
L26	295	(destabilizing or stability) adj20 (pest or n-end or n-terminal or ubiquitin)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:59
L27	334	(destabilizing or stability) adj20 (pest or n-end or n-terminal or ubiquitin)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:59
L28	2	(destabilizing or stability) adj20 (pest or n-end or n-terminal or ubiquitin) and renilla adj5 luciferase	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 06:01
L29	36	cyclin adj destruction adj box	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:14
L30	0	protein adj degradation same sequence	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 06:02
L31	3077	protein adj degradation	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 06:22

L32	102	I31 and (I27 or I29)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 06:18
L33	2	I32 and renilla adj5 luciferase	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 06:09
L34	691	mRNA adj degradation	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 06:09
L35	104	I31 and (I27 or I29 or ssrA)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 06:22
L36	5071	protein adj (degradation or instability ot stability)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 06:22
L37	158	I36 and (I27 or I29 or ssrA)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 06:23
L38	11882	protein adj5 (degradation or instability ot stability or degraded)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 07:51
L39	206	I38 and (I27 or I29 or ssrA)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 06:23
L40	71	I38 same (I27 or I29 or ssrA)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 06:23
L41	4	I39 and renilla adj5 luciferase	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 06:23

L42	4	I39 and renilla same luciferase	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 06:23
L43	8	I39 and promoterless	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 06:23
L44	384	destabilizing adj element or c-fos adj ARE or AU adj rich or aure or dst adj (element or sequence)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:35
L45	11800	protein adj5 (degradation or instability or stability or degraded)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 07:51
L46	66	I44 and I45	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:12
L47	29	I46 and luciferase	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:10
L48	123	fusion adj10 (luciferase or GFP or lux or luc) same (marker and kanamycin or neomycin or resistance)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 07:54
L49	13	fusion adj10 (luciferase or GFP or lux or luc) adj10 (marker and kanamycin or neomycin or resistance)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:06
L51	3	fusion adj10 (luciferase or GFP or lux or luc) adj10 (marker and kanamycin or neomycin or resistance) and N adj gene	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 07:58
L52	4	fusion adj10 (luciferase or GFP or lux or luc) adj10 (marker and kanamycin or neomycin or resistance) and renilla	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:06

L53	4	I44 and I39	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:14
L54	36527	cyclin adj destruction adj box or pest or (n-end or n-terminal) adj10 degradation or ubiquitin or ssra	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:36
L55	39	I44 and I54	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:18
L56	27	(I44 and I54) and reporter	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:18
L57	1	rapid adj decay same (mRNA or RNA) adj5 instability	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:29
L58	12	rapid adj decay and elements same (mRNA or RNA) adj5 instability	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:30
L59	3	rapid adj decay and elements adj5 instability	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:30
L60	20	rapid adj decay and elements same instability	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:30
L61	2606	RNA same elements same instability	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:30
L62	96	RNA same elements same instability	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:31

L63	4	RNA same elements same instability and protein adj degradation	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:33
L64	11	elements same instability and protein adj degradation	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:32
L65	7	I64 not I63	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:32
L66	4	I44 and instability and protein adj degradation	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:33
L67	8	I44 and protein adj degradation	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:36
L68	2217	Daly.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:35
L69	2	Daly.in. and I44	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:35
L70	384	destabilizing adj element or c-fos adj ARE or AU adj rich or aure or dst adj (element or sequence) or AURE	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:36
L71	621	destabilizing adj element or c-fos adj ARE or AU adj rich or aure or dst adj (element or sequence) or AURE or ARE	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:36
L72	8	I71 and protein adj degradation	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:36

L73	44	(cyclin adj destruction adj box or pest or (n-end or n-terminal) adj10 degradation or ubiquitin or ssra) and l71	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:37
L74	28	(cyclin adj destruction adj box or pest or (n-end or n-terminal or ubiquitin) adj10 degradation or ssra) and l71	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 08:37

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	0	pmon505-70	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:17
L2	0	pmon%	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:19
L3	59062	pmo\$	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:19
L4	882	pmon\$	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:19
L5	450	pmon\$ same plant	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:19
L6	43	pmon\$ same plant same reporter	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:35
L7	3	09/960454 and pest	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:39
L8	0	09/960454 and destabilizing	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:36
L9	3	09/960454 and stability	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:36
L10	1	10/151750 and (PEST or stability)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2004/12/03 05:40

# STN Columbus

ENTER L# LIST OR (END):l14  
'REML14' IS NOT VALID. VALID FILE NAMES ARE 'MEDLINE, CAPLUS'  
You have entered a file name of duplicates to keep that is not  
referenced by any of the L#s specified for this DUPLICATE command.  
The file names of duplicates that can be kept are listed above.  
Please enter one of these file names.

=> dup rem l14  
PROCESSING COMPLETED FOR L14  
L15 9 DUP REM L14 (0 DUPLICATES REMOVED)

=> s l15 adn py<=2001  
MISSING OPERATOR L15 ADN  
The search profile that was entered contains terms or  
nested terms that are not separated by a logical operator.

=> s l15 and py<=2001  
2 FILES SEARCHED...  
L16 2 L15 AND PY<=2001

=> d ibib ab s1-2  
'S1-2' IS NOT A VALID FORMAT  
In a multifile environment, a format can only be used if it is valid  
in at least one of the files. Refer to file specific help messages  
or the STNGUIDE file for information on formats available in  
individual files.  
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):filedefault

L16 ANSWER 1 OF 2 MEDLINE on STN  
Full Text  
AN 2001652528 MEDLINE  
DN PubMed ID: 11555652  
TI Proteasome-mediated glucocorticoid receptor degradation restricts  
transcriptional signaling by glucocorticoids.  
AU Wallace A D; Cidlowski J A  
CS Molecular Endocrinology Group, Laboratory of Signal Transduction, NIEHS,  
National Institutes of Health, Research Triangle Park, North Carolina  
27709, USA.  
SO Journal of biological chemistry, (2001 Nov 16) 276 (46) 42714-21.  
Journal code: 2985121R. ISSN: 0021-9258.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200112  
ED Entered STN: 20011114  
Last Updated on STN: 20030105  
Entered Medline: 20011226

=> d ibib abs 1-2

L16 ANSWER 1 OF 2 MEDLINE on STN  
Full Text  
ACCESSION NUMBER: 2001652528 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11555652  
TITLE: Proteasome-mediated glucocorticoid receptor degradation  
restricts transcriptional signaling by glucocorticoids.  
AUTHOR: Wallace A D; Cidlowski J A  
CORPORATE SOURCE: Molecular Endocrinology Group, Laboratory of Signal  
Transduction, NIEHS, National Institutes of Health,  
Research Triangle Park, North Carolina 27709, USA.

STN Columbus

SOURCE: Journal of biological chemistry, (2001 Nov 16) 276 (46)  
42714-21.

Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200112

ENTRY DATE: Entered STN: 20011114

Last Updated on STN: 20030105

Entered Medline: 20011226

AB Ligand-dependent down-regulation of the glucocorticoid receptor (GR) has been shown to limit hormone responsiveness, but the mechanisms involved in this process are poorly understood. The glucocorticoid receptor is a phosphoprotein that upon ligand binding becomes hyperphosphorylated, and recent evidence indicates that phosphorylation status of the glucocorticoid receptor plays a prominent role in receptor protein turnover. Because phosphorylation is a key signal for ubiquitination and proteasomal catabolism of many proteins, we evaluated whether the ubiquitin-proteasomal pathway had a role in glucocorticoid receptor down-regulation and the subsequent transcriptional response to glucocorticoids. Pretreatment of COS-1 cells expressing mouse glucocorticoid receptor with the proteasome inhibitor MG-132 effectively blocks glucocorticoid receptor protein down-regulation by the glucocorticoid dexamethasone. Interestingly, both MG-132 and a second proteasome inhibitor beta-lactone significantly enhanced hormone response of transfected mouse glucocorticoid receptor toward transcriptional activation of glucocorticoid receptor-mediated reporter gene expression. The transcriptional activity of the endogenous human glucocorticoid receptor in HeLa cells was also enhanced by MG-132. Direct evidence for ubiquitination of the glucocorticoid receptor was obtained by immunoprecipitation of cellular extracts from proteasome-impaired cells. Examination of the primary sequence of mouse, human, and rat glucocorticoid receptor has identified a candidate PEST degradation motif. Mutation of Lys-426 within this **PEST element** both abrogated ligand-dependent down-regulation of glucocorticoid receptor protein and simultaneously enhanced glucocorticoid receptor-induced transcriptional activation of gene expression. Unlike wild type GR, proteasomal inhibition failed to enhance significantly transcriptional activity of K426A mutant GR. Together these findings suggest a major role of the ubiquitin-proteasome pathway in regulating glucocorticoid receptor protein turnover, thereby providing a mechanism to terminate glucocorticoid responses.

L16 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

Full Text

ACCESSION NUMBER: 2000:421327 CAPLUS

DOCUMENT NUMBER: 133:73006

TITLE: Enhanced protein production in higher plants by N-terminal fusion of a ubiquitin or a cucumber mosaic virus coat protein peptide

INVENTOR(S): Fang, Rong-xiang; Wu, Jung-lin; Chen, Xiao-ying

PATENT ASSIGNEE(S): Institute of Molecular Agrobiology, Singapore

SOURCE: PCT Int. Appl., 42 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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STN Columbus

WO 2000036129	A1	20000622	WO 1998-SG103	19981211 <--
W: CN, JP, SG, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1137787	A1	20011004	EP 1998-961712	19981211 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002532098	T2	20021002	JP 2000-588378	19981211
PRIORITY APPLN. INFO.:			WO 1998-SG103	W 19981211
AB Methods are disclosed for enhancing protein prodn. in plant cell or plant. One method comprises prep. a vector by inserting a gene encoding ubiquitin in front of a gene encoding a protein of interest and inserting the vector into a cell. A fusion protein will be expressed which includes ubiquitin plus the protein of interest. Ubiquitin C-terminal hydrolases can cleave the fusion protein leaving the desired protein in its free state. This method causes enhanced prodn. of the protein of interest as compared to performing the same method without the ubiquitin gene as part of the vector. A ubiquitin promoter is unnecessary to yield this enhanced prodn. and is not used. A second method is very similar except that in place of a ubiquitin gene, a gene encoding fourteen amino acids of cucumber mosaic virus coat protein is inserted in front of the gene of interest. This results in expression of a fusion protein comprising the fourteen amino acid residues of the coat protein bonded to the protein of interest. The fusion protein is produced at a higher level than is the protein when the coat protein gene fragment is not present in the vector. In both methods the genes can be placed under the control of heterologous promoters such as a 35S promoter. The method was exemplified by expression of ubiquitin or CMV coat protein peptide fusion proteins with $\beta$ -glucuronidase or luciferase in tobacco. The fusion protein expression was driven by the CaMV 35S promoter. CMV coat protein peptide was more efficient in enhancing the expression of fusion proteins than ubiquitin.				
REFERENCE COUNT:	4	THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		

=> s daly?/au and reporter and instability  
L17            0 DALY?/AU AND REPORTER AND INSTABILITY

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L18            3 DALY?/AU AND REPORTER AND AU (A) RICH

=> d ibib abs 1-3

L18 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

Full Text

ACCESSION NUMBER: 2004:493515 CAPLUS  
DOCUMENT NUMBER: 141:48556  
TITLE: Constructs for gene expression analysis and gene regulation assays and use for drug screening  
INVENTOR(S): Daly, John  
PATENT ASSIGNEE(S): Australia  
SOURCE: U.S. Pat. Appl. Publ., 70 pp., Cont.-in-part of Appl.  
No. PCT/AU02/00351.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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STN Columbus

US 2004115704	A1	20040617	US 2003-658093	20030909
US 2004209274	A2	20041021		
WO 2002072844	A1	20020919	WO 2002-AU351	20020308
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2001-274770P	P 20010309
			WO 2002-AU351	A2 20020308

AB The present invention relates generally to constructs and their use in gene expression or gene regulation assays. More particularly, the present invention provides expression vectors and/or reporter vectors providing kinetics of protein expression with improved temporal correlation to promoter activity. Even more particularly, the invention provides expression vectors comprising a transcribable polynucleotide which comprises a sequence of nucleotides encoding a RNA element that modulates the stability of a transcript corresponding to the transcribable polynucleotide. The present invention provides, inter alia, novel vectors, useful for identifying and analyzing cis- and trans-acting regulatory sequences/factors as well as vectors and genetically modified cell lines or organisms that are particularly useful for drug screening and drug discovery.

L18 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

Full Text

ACCESSION NUMBER: 2002:716495 CAPLUS  
 DOCUMENT NUMBER: 137:243082  
 TITLE: Expression vectors which modulate the stability of transcripts in combination with destabilization of protein for use in post-transcriptional and post-translational reporter assays  
 INVENTOR(S): Daly, John  
 PATENT ASSIGNEE(S): Gene Stream Pty. Ltd., Australia  
 SOURCE: PCT Int. Appl., 103 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002072844	A1	20020919	WO 2002-AU351	20020308
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2440148	AA	20020919	CA 2002-2440148	20020308
EP 1373528	A1	20040102	EP 2002-708018	20020308
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

STN Columbus

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004530425	T2	20041007	JP 2002-571895	20020308
US 2004115704	A1	20040617	US 2003-658093	20030909
US 2004209274	A2	20041021		
PRIORITY APPLN. INFO.:			US 2001-274770P	P 20010309
			WO 2002-AU351	W 20020308

AB The present invention relates generally to expression vectors and their use in gene expression or gene regulation assays. The present invention provides expression vectors which modulate the stability of transcripts and consequently, the amt. of protein produced by the vector. Although expression vectors which increase the stability of a transcript are clearly encompassed by the present invention, a particularly preferred embodiment focuses on destabilizing transcripts. Here transcript stability can be reduced by the addn. of one or more destabilizing elements (e.g. AU-rich and/or U-rich elements) to, or by the removal of one or more stability elements (e.g., a poly A tail) from, a transcribable polynucleotide. Another aspect of the present invention contemplates the combination of a protein destabilizing element (e.g., a DNA/RNA sequence encoding an intracellular protein degrdn. signal or degron which may be selected from a destabilizing amino acid at the amino-terminus of a polypeptide of interest, a PEST region or a ubiquitin) and an mRNA destabilizing element, such that both mRNA and protein are destabilized. Compared to existing expression vectors, the vector of the present invention provides kinetics of protein expression with improved temporal correlation to the promoter activity, e.g., by reducing the time lag between decreased promoter activity and decreased levels of a corresponding expression product. Vectors of the present invention are useful for identifying and analyzing cis- and trans-acting regulatory sequences/factors as well as vectors and genetically modified cell lines or organisms that are particularly useful for drug screening and drug discovery.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 3 SCISEARCH COPYRIGHT (c) 2004 The Thomson

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\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Despite promoting growth in many cell types, epidermal growth factor (EGF) induces growth inhibition in a variety of cancer cells that overexpress its receptor. The cyclin-dependent kinase inhibitor p21(WAF1) is a central component of this pathway. We found in human MDA-468 breast cancer cells that EGF up-regulates p21(WAF1) mRNA and protein, through a combination of increased mRNA stability and transcription. The decay rate of a hybrid luciferase **reporter** full-length p21(WAF1) 3'-untranslated region (UTR) mRNA was significantly faster than that of a control mRNA. Transfections with a variety of p21(WAF1) 3'-UTR constructs identified multiple cis-acting elements capable of reducing basal **reporter** activity. Short wavelength ultraviolet light induced **reporter** activity in constructs containing the 5' region of the p21(WAF1) 3'-UTR, whereas EGF induced **reporter** activity in constructs containing sequences 3' of the UVC-responsive region. These cis-elements bound multiple proteins from MDA-468 cells, including HuR and poly(C)-binding protein 1 (CP1). Immunoprecipitation studies confirmed that HuR and CP1 associate with p21(WAF1) mRNA in MDA-468 cells. Over- and underexpression of HuR in MDA-468 cells did not affect EGF-induced p21(WAF1) protein expression or growth inhibition. However, binding of HuR to its target 3'-UTR cis-element was regulated by UVC but not by EGF, suggesting that these stimuli modulate the stability of p21(WAF1) mRNA via different mechanisms. We conclude that EGF-induced p21(WAF1) protein expression is mediated largely by stabilization of p21(WAF1) mRNA elicited via multiple 3'-UTR cis-elements. Although HuR binds at least one of these elements, it does not appear to be a major modulator of p21(WAF1) expression or growth inhibition in this system. CP1 is a novel p21(WAF1) mRNA-binding protein that may function cooperatively with other mRNA-binding proteins to regulate p21(WAF1) mRNA stability.

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